

Amended
claimed in claim 1, [~~to skin in need of said treatment~~] together with a pharmaceutically acceptable additive.

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7. (Amended) A corticoid 17,21-dicarboxylic ester or corticosteroid 17-carboxylic ester 21-carbonic ester of the formula I as claimed in claim 1, wherein R(1), A, Y, Z[,] and R(3) [and R(4)] are defined as in claim 1, and wherein R(2) is

Kindly enter the following claim:

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--8. A pharmaceutical composition as claimed in claim 4 for treating dermatoses which are inflammatory and allergic.--

REMARKS

Claims 4, 5, and 7 have been amended to more clearly define that which applicants consider to be their invention. Claim 8 has been added to recite the limitation deleted from claim 4.

The Examiner's comments on Election/Restriction and the requirement being made FINAL are noted. Applicants acknowledge the Examiner's statement that upon allowance of the compound claims, process claims reciting compounds of the same scope as the allowed compounds would be rejoined.

Claim 7 is rejected under 35 U.S.C. § 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements, citing MPEP § 2172.01. The Examiner states that the omitted elements are: the identification and definition of R(4), noting that claim 7 recited "wherein R(1), A, Y, Z, R(3) and R(4) are defined as in

claim 1" although the structure of formula I as defined by claim 1 does not identify or define R(4) as recited by claim 7.

Claim 7 has been amended to delete the recitation of R(4). This rejection has been overcome and should be withdrawn.

With regard to the claim rejections under 35 U.S.C. §§ 102(b) and 103, applicants acknowledge the Examiner's statements on page 4 of the Office action:

the rejection of claims 1-2 and 4-5 under 35 USC 102(b) over Kamano et al. ('172) has been withdrawn;

the rejection of claims 1-2 and 4-5 under 35 USC 103(a) over Villax et al. ('693) has been withdrawn;

the rejection of claims 1-2 and 4-5 under 35 USC 103(a) over Kamano et al. ('172) has been withdrawn;

the rejection of claims 1-2 and 4-5 under 35 USC 103(a) over Annen et al. ('451) has been withdrawn; and

the rejection of claim 2 under 35 USC 103(a) over Page et al. ('971) was made moot by the cancellation of the instant claim.

Claims 1 and 4-5 remain rejected under 35 U.S.C. § 103(a) over Page et al. and claim 7 is added to this rejection. This rejection is respectfully traversed.

The Examiner discusses Page et al. in the paragraph bridging pages 5 and 6 of the Office action and indicates that the compounds in Examples 9 and 19 are most pertinent. It is contended that these compounds, betamethasone-17-benzoate and

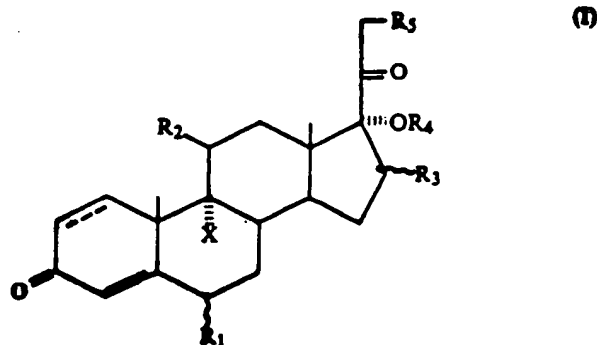
betamethasone-17-valerate-21-acetate, differ from the instant compounds by the presence of a hydroxyl or an acetate in the 21-position, respectively, and that the reference teaches an equivalence between a hydroxyl/group and an acyl group in the 21-position and an equivalence between acyl groups having an alkyl and an aralkyl moiety at col. 1, lines 17-55.

As pointed out to the Examiner on page 4 of the March 18, 1998 amendment, in claim 1 herein, R(1) is defined as unsubstituted phenyl or phenyl substituted by one to three substituents selected from the group consisting of methoxy, chlorine, fluorine, methyl, trifluoromethyl, acetamino, acetaminomethyl, t-butoxy, t-butyl, 3,4-methylenedioxy, BOC-amino, amino and dimethylamino as disclosed at page 65, lines 11-21 of the specification. Similarly, in claim 1, n is zero, and (C₁-C₄)-alkyl is defined only as saturated, branched by further alkyl groups with m being 1. Thus, the 21-side chain effectively becomes -O-CO-[(C₁-C₄)-alkyl]-phenyl, with the phenyl being unsubstituted or substituted as defined in claim 1. This has the effect that esters, i.e., 21-phenyl carboxylates, including (substituted) 21-phenyl acetates and propionates are claimed.

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Page et al. ('971) teach a process for the preparation of esters of the formula I



in which numerous definitions for the substituents R_1 , R_2 , R_3 , R_4 , R_5 , and X are disclosed. The R_5 substituent of Page et al. corresponds to the portion of the side chain in position 21 of the presently claimed esters beginning with the oxygen following the CH_2 group. R_5 of Page et al. can be, *inter alia*, also R_6 ; and R_6 can be, *inter alia*, OR_7 , where R_7 is an acyl group of the formula $R'CO$ with R' being, *inter alia*, (ii) an aralkyl group of 7 or 8 carbon atoms (see the Abstract and col. 21, lines 1-40). As pointed out of record, by following this complicated procedure, it might be possible to construe a compound such as a 21-phenyl acetate or 21-phenyl propionate. However, there is no teaching or suggestion in the reference to modify the molecule in this very particular manner, especially in view of the multiple possibilities. In addition, a similar very special selection would have to be made with respect to R_4 of the reference, from which the variant (iii) i.e., a phenyl group, would have to be

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simultaneously chosen. As set forth in MPEP § 2143.01, the fact that a reference **can** be modified is not sufficient to establish *prima facie* obviousness.

The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. *In re Mills*, 916 F.2d 680, 16 USPQ2d 1430 (Fed. Cir. 1990).

The Examiner acknowledges the applicants' argument of record on page 5 of the Office action, but finds it unpersuasive, noting that a reference is not limited to its working examples but must be evaluated for what it teaches those of ordinary skill in the art, citing *In re Boe*, 355 F.2d 961, 148 USPQ 507 (CCPA 1996), and *In re Chapman*, 357 F.2d 418, 148 USPQ 711 (CCPA).

It is the applicants' position that neither of these decisions involves a factual situation apposite to that herein. In *Boe*, the appealed claims were directed to a method of manufacturing highly porous absorptive non-woven materials in the nature of chamois leather. Such materials have good water retention as well as absorptive properties. The rejection involved combining the teachings of two cited references. In *Chapman*, the appealed claims were directed to high strength chlorinated polyethylenes and process for preparing them. Claim 1, directed to the product, read:

1. A chlorinated polyethylene resin
having a chlorine content between about 25%

and about 65% by weight, molecular weight characteristics such that its intrinsic viscosity as measured in o-dichlorobenzene at 100° C. is not less than about 1.8, chemically inert, insoluble in organic solvents at 20-25° C., having a tensile strength value according to ASTM method D-638-58T of at least about 3,000 and equal to at least about 100 times the weight percent chlorine in the resin, having a true ultimate tensile value of at least about 8,000, and having an infrared spectrogram showing characteristic absorption peaks at the following wave length: 3.42 to 3.5 microns; 3.38 to 3.48 microns; 6.8 to 6.9 microns; and at 7.8 to 7.9 microns.

Thus, neither decision dealt with claims directed to compounds such as the corticoid esters of the present invention, or to compounds defined by a generic chemical formula such as formula I herein. Moreover, these matters both were decided in 1966. However, the Office has established "Genus-Species Guidelines" to assist in the examination of claims directed to a species of chemical compositions based, as herein, on a single prior art reference and the same are set forth in MPEP § 2144.08. As therein stated:

The fact that a claimed compound may be encompassed by a disclosed generic formula does not by itself render that compound obvious. *In re Baird*, 16 F.3d 380, 382, 29 USPQ2d 1550, 1552 (Fed. Cir. 1994).

The prior art must teach a motivation or suggestion to make the claimed invention. In a case wherein the prior art discloses a genus, the Examiner should consider, *inter alia*, the number of species encompassed by the genus taking into consideration all of

the variables possible. Considering the number of variables, and particularly those of R_4 , R_5 , R_6 , and R_7 , the number of species encompassed by Page et al. formula I is large indeed. In all cases, and in accordance with MPEP § 2144.08, the Examiner should determine whether one of ordinary skill in the relevant art would have been motivated to make the claimed invention as a whole, i.e., to select the claimed species or subgenus from the disclosed prior art genus.

[A] *prima facie* case of unpatentability requires that the teachings of the prior art suggest *the claimed compounds* to a person of ordinary skill in the art. *In re Deuel*, 51 F.3d 1552 at 1557 (emphasis in original).

Here, Page et al. do not reasonably suggest the claimed compounds. Applicants have scrutinized the reference and find no teaching of a compound having a phenyl substituent in the R(1) position of the presently claimed compounds. In fact, all of the reference examples refer to aliphatic group substituents such as acetyl or propionyl. Thus, one skilled in the art would not be motivated by the teachings of Page et al., as the single cited reference, to prepare the presently claimed compounds.

As further set forth in MPEP § 2143.01, a statement that modifications of the prior art to meet the claimed invention would have been "well within the ordinary skill of the art at the time the claimed invention was made," or as stated by the Examiner herein "obvious to the ordinary artisan," because the

reference relied upon teaches that all aspects of the claimed invention were individually known in the art, is not sufficient to establish a *prima facie* case of obviousness without some objective reason to combine the teachings, citing *Ex parte Levengood*, 28 USPQ2d 1300 (Bd. Pat. App. & Inter. 1993). Applicants find no such objective reason in Page et al., especially since specific selections from amongst all the numerous variables of R_4 , R_5 , R_6 , and R_7 would need to be made.

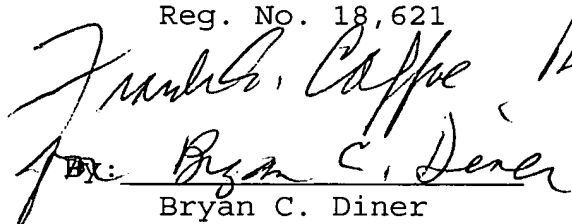
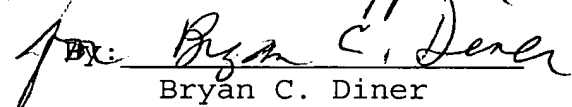
The Examiner has failed to establish a *prima facie* case of obviousness. This rejection is in error and should be withdrawn.

In view of the amendments to the claims and in light of the above remarks, it is urged that this application is in condition for allowance. An early and favorable action is earnestly solicited.

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